

AMENDMENTS TO THE CLAIMS

1. (Currently amended) A device for non-invasive measurement of the individual metabolic rate of an individual substantially spherical metabolizing particle, which device comprises

- a) at least one compartment, said at least one compartment being defined by a diffusion barrier and said at least one compartment being capable of retaining a medium with a substantially spherical metabolizing particle, said diffusion barrier is arranged around the substantially spherical metabolizing particle to restrict and reduce the diffusive flux of metabolites to and from the particle, allowing metabolite transport through the diffusion barrier to the substantially spherical metabolizing particle by means of diffusion wherein the medium within the compartment is stagnant so that the medium cannot mix by turbulent flow and so that a linear metabolite diffusion gradient is established from the substantially spherical metabolizing particle and throughout the medium in said at least one compartment,
- b) at least one detector for measuring the concentration of a metabolite inside the compartment, the transverse dimension of said compartment being less than 1.5 millimeter,

wherein transport of metabolites to and/or from said particle through said medium in said at least one compartment occurs only through diffusion.

2. (Previously presented) The device according to claim 1, wherein the diffusion barrier is constituted by at least one compartment wall having at least one metabolite permeable opening.

3. (Previously presented) The device according to claim 2, wherein the at least one compartment wall is produced from a substantially metabolite impermeable material.

4-7 (Canceled)

8. (Previously presented) The device according to claim 1, wherein the diffusion barrier is constituted by a medium with a viscosity above or equal to that of water.

9. (Canceled)

10. (Previously presented) The device according to claim 1, wherein the shape of the compartment is selected from the group consisting of a cylinder, a polyhedron, a cone, a hemisphere or a combination thereof.

11. (Canceled)

12. (Previously presented) The device according to claim 1 comprising an insert for the adjustment of the transverse dimension of the compartment.

13. (Previously presented) The device according to claim 1, wherein the compartment has an adjustable bottom operable to change the dimensions and either increase or decrease the compartment volume.

14-20 (Canceled)

21. (Previously presented) The device according to claim 1, wherein a metabolite permeable layer is arranged in the bottom of the at least one compartment.

22-26 (Canceled)

27. (Withdrawn) The method according to claim 21, wherein a metabolite permeable layer is placed between the substantially spherical metabolizing particle and the metabolite detector.

28-29 (Canceled)

30. (Previously presented) The device according to claim 1, wherein the metabolite is oxygen or carbon dioxide.

31. (Previously presented) The device according to claim 1, wherein the detector is an oxygen detector.

32-35 (Canceled)

36. (Withdrawn) A non-invasive method for determining the metabolic rate of a substantially spherical metabolizing particle, comprising

- a) providing at least one device as defined in claim 1,
- b) arranging a substantially spherical metabolizing particle in the medium of a compartment,
- c) measuring a metabolite concentration inside the compartment obtaining a metabolite concentration measure, and
- d) correlating said metabolite concentration measure to a metabolic rate of said substantially spherical metabolizing particle.

37. (Withdrawn) The method according to claim 36, wherein metabolite is supplied to the substantially spherical metabolizing particle by diffusion through the medium.

38. (Withdrawn) The method according to claim 36, wherein the substantially spherical metabolizing particle is cultured in the compartment.

39. (Canceled)

40. (Withdrawn) The method according to claim 36, wherein the metabolic rate of said substantially spherical metabolizing particle is determined by determining a metabolite diffusion gradient in the compartment based on the measured metabolite concentration, and

correlating said metabolite diffusion gradient to the metabolic rate of said substantially spherical metabolizing particle.

41. (Canceled)

42. (Withdrawn) The method according to claim 36, wherein the metabolite concentration is a gas partial pressure.

43. (Withdrawn) The method according to claim 42, wherein the gas partial pressure is the partial pressure of oxygen or carbon dioxide.

44. (Canceled)

45. (Withdrawn) The method according to claim 36, wherein the substantially spherical metabolizing particle is selected from the group consisting of an embryo, at least one cancer cell, at least one stem cell, embryonal stem cells, *C. elegans* and multicellular organisms.

46-47 (Canceled)

48. (Withdrawn) A method for regulating metabolite supply to a substantially spherical metabolizing particle during culturing, comprising

a) providing at least one device comprising a compartment with a medium,

- b) culturing a substantially spherical metabolizing particle in the medium of the compartment,
- c) measuring a metabolite concentration inside the compartment obtaining a metabolite concentration measure, and optionally
- d) correlating said metabolite concentration measure to a metabolic rate of said substantially spherical metabolizing particle and optionally
- e) regulating the metabolite supply depending on the metabolite concentration measure and/or the metabolic rate of said substantially spherical metabolizing particle.

49. (Withdrawn) The method according to claim 48, wherein at least one of the devices is as defined in claim 1.

50. (Canceled)

51. (Withdrawn) The method according to claim 48, wherein the metabolite is oxygen and the metabolic process is respiration.

52. (Withdrawn) The method according to claim 48, wherein the regulation is conducted by changing the metabolite concentration outside the compartment.

53. (Withdrawn) The method according to claim 48, wherein the regulation is conducted by changing the dimensions of the compartment.

54-56 (Canceled)

57. (Withdrawn) The method according to claim 48, wherein the regulation is conducted by changing the diffusion barrier of the compartment.

58-59 (Canceled)

60. (Withdrawn) A method for selecting a viable embryo comprising,

- a) determining the metabolic rate of the embryo at least once during culturing , and
- b) selecting the embryo having an optimal metabolic rate.

61. (Withdrawn) The method according to claim 60, wherein the determination of the metabolic rate is conducted without causing any change in the growth conditions experienced by the embryo.

62. (Withdrawn) The method according to claim 60, wherein the metabolic rate is measured in a device as defined by claim 1.

63. (Withdrawn) The method according to claim 60, wherein the metabolic rate is determined by a method as defined in claim 36.

64. (Withdrawn) A non-invasive method for determining the metabolic rate of a metabolizing particle, comprising

- a) providing at least one device as defined in claim 1,
- b) culturing a metabolizing particle in the medium of a compartment,
- c) reducing metabolite supply to the medium during at least a part of the culturing period,
- d) measuring a metabolite concentration inside the compartment obtaining a metabolite concentration measure after the metabolite supply has been reduced, and
- e) correlating said metabolite concentration measure to a metabolic rate of said substantially spherical metabolizing particle.

65. (Withdrawn) The method according to claim 64, wherein the metabolite is oxygen and the metabolic rate is the respiration rate.

66. (Withdrawn) The method according to claim 64, wherein the oxygen supply is reduced to zero.

67. (Withdrawn) The method according to claim 64, wherein the gas partial pressure measure in the compartment has been obtained during the period of reduced oxygen supply.

68. (Previously presented) A culture device for culturing a metabolizing particle, which device comprises at least one compartment, said at least one compartment being defined

by a diffusion barrier and said at least one compartment being capable of retaining a medium with a metabolizing particle, said at least one compartment having a transverse dimension which does not exceed 1.5 millimeter, so that said medium is stagnant and so that the medium cannot mix by turbulent flow, said diffusion barrier allowing metabolite transport to and/or from the metabolizing particle solely by means of diffusion, whereby a metabolite diffusion gradient is established from the metabolizing particle and throughout the medium in said at least one compartment, wherein transport of metabolites to and/or from said particle through said medium in said at least one compartment occurs solely through diffusion.

69. (Canceled)

70. (Withdrawn) A method for culturing a metabolizing particle, said method comprising

- a) providing at least one device as defined in claim 68,
- b) arranging a metabolizing particle in the medium of the compartment, and
- c) culturing the metabolizing particle.

71. (Previously presented) The device according to claim 2, wherein the metabolite permeable opening is constituted by a metabolite permeable membrane.